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10/649,719	08/28/2003	Kenji Nakajima	Q77115	6178

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EXAMINER	
LAM, ANN Y	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 05/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/649,719	NAKAJIMA, KENJI	
	Examiner	Art Unit	
	Ann Y. Lam	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/30/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 7 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, recites the limitation "the time" in line 21. There is insufficient antecedent basis for this limitation in the claim.

Claim 2, recites the limitation "the forcible flowing" in line 5. There is insufficient antecedent basis for this limitation in the claim.

Claim 2, recites the limitation "the period of time" in line 6. There is insufficient antecedent basis for this limitation in the claim.

Claim 3, recites the limitation "the time" in line 21. There is insufficient antecedent basis for this limitation in the claim.

Claim 3, recites the limitation "the time" in line 32. There is insufficient antecedent basis for this limitation in the claim.

Claim 4, recites the limitation "the forcible flowing" in line 5. There is insufficient antecedent basis for this limitation in the claim.

Claim 4, recites the limitation "the period of time" in line 6. There is insufficient antecedent basis for this limitation in the claim.

Claim 7, recites the limitation "the forcible flowing" in line 6. There is insufficient antecedent basis for this limitation in the claim.

Claim 7, recites the limitation "the period of time" in line 7. There is insufficient antecedent basis for this limitation in the claim.

Claim 8, recites the limitation "the forcible flowing" in line 6. There is insufficient antecedent basis for this limitation in the claim.

Claim 8, recites the limitation "the period of time" in line 7. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

1. Claims 5-8 are rejected under 35 U.S.C. 102(e) as being anticipated by Shipwash, 6,846,638.

As to claim 5, Shipwash disclose a reaction apparatus comprising:

i) a reaction vessel (i.e., microfluidic system in col. 21, lines 52-53; and see col. 40, lines 63-67, disclosing channels, chambers or wells), which is provided with a support section (i.e., the channels, chambers or wells, col. 40, line 67, which contain

beads) for releasably (i.e., capable of releasing) supporting a biochemical analysis unit within the reaction vessel, the biochemical analysis unit being provided with a plurality of porous adsorptive regions (i.e., the porous resins, or alternatively, the regions containing the porous resins, are considered to be a plurality of adsorptive regions, col. 40, line 63 – col. 41, line 3), to which ligands or receptors have been bound respectively (col. 40, line 67 – col. 41, line 2, disclosing immobilization of proteins or nucleic acids onto the porous resins),

ii) flowing means (i.e., micropumps and/or microvalves, col. 20, lines 57-58) capable of causing a reaction liquid containing an enzyme-labeled antibody to flow within the reaction vessel (see col. 28, line 66 – col. 29, line 23, and see also col. 20, col. 21, lines 23-41, disclosing pumps for pressurized flow through through microchannels for incubation and washing steps).

The Office notes that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In this case, Shipwash disclose the structural limitations as previously described and the structural limitations are capable of performing the intended use. More specifically, as to claim 5, the support section (i.e., the channels, chambers or wells, col. 40, line 67, which contain beads) is considered to be releasably supporting a biochemical analysis unit (i.e., the beads) within the reaction vessel because it supports the beads and it is capable of releasing the beads (by any means). The Office notes that Applicant has not

recited how the support section may release the biochemical analysis. Also, the reaction vessel disclosed by Shipwash is capable of performing the intended use recited by Applicant. That is, the reaction vessel is capable of allowing specific binding of a labeled receptor or a labeled ligand, which has been labeled with a labeling substance and has been specifically bound to at least one of the ligands or at least one of the receptors, and an enzyme-labeled antibody with each other, because the reaction vessel contains porous resins to which proteins or nucleic acids may be immobilized (col. 40, line 63 – col. 41, line 3). Also, the flowing means (i.e., micropumps, col. 20, lines 57-58) disclosed by Shipwash is capable of forcibly causing the reaction liquid containing the enzyme-labeled antibody to flow such that the reaction liquid containing the enzyme-labeled antibody flows across each of the porous adsorptive regions of the biochemical analysis unit, because Shipwash disclose that the micropumps are capable of producing pressurized flow through the device for incubation and washing steps.

As to claim 6, the flowing means (i.e., micropumps, col. 20, lines 57-58) disclosed by Shipwash is also capable of forcibly causing a reaction liquid containing the labeled receptor or the labeled ligand, which has been labeled with the labeling substance, to flow such that the reaction liquid containing the labeled receptor or the labeled ligand flows across each of the porous adsorptive regions of the biochemical analysis unit, because Shipwash disclose that the micropumps are capable of producing pressurized flow through the device for incubation and washing steps (col. 21, lines 23-41).

Likewise, as to claim 7, the flowing means (i.e., micropump and/or microvalves, col. 20, lines 57-58) disclosed by Shipwash is capable of operating such that, after the reaction liquid containing the enzyme-labeled antibody has been forcibly caused to flow such that the reaction liquid flows across each of the porous adsorptive regions of the biochemical analysis unit, the forcible flowing is ceased during a period of time longer than the period of time during which the reaction liquid containing the enzyme-labeled antibody has been forcibly caused to flow, because Shipwash discloses that the micropumps and microvalves allow for precise control of pressurized flow (col. 20, lines 56-57; and col. 21, lines 30-33). That is, the micropumps and microvalves disclosed by Shipwash are capable of ceasing flow across the biochemical analysis unit.

Similarly, as to claim 8, the flowing means (i.e., micropumps and microvalves, col. 20, lines 57-58) is capable of operating such that, after the reaction liquid containing the enzyme-labeled antibody has been forcibly caused to flow such that the reaction liquid flows across each of the porous adsorptive regions of the biochemical analysis unit, the forcible flowing is ceased during a period of time longer than the period of time during which the reaction liquid containing the enzyme-labeled antibody has been forcibly caused to flow, because Shipwash discloses that the micropumps and microvalves allow for precise control of pressurized flow (col. 20, lines 56-57; and col. 21, lines 30-33). That is, the micropumps and microvalves disclosed by Shipwash are capable of ceasing flow across the biochemical analysis unit.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claim 1 and 3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shipwash, 6,846,638, in view of Decker et al., 4,230,683.

Shipwash discloses the invention substantially as claimed.

More specifically, as to claim 1, Shipwash discloses a chemical luminescence method (col. 26, lines 20-23, and col. 19, lines 50-55) comprising the steps of:

i) obtaining a biochemical analysis unit (i.e., microarray and microfluidic system in col. 21, lines 52-53) provided with a plurality of porous adsorptive regions (col. 40, line 63 – col. 41, line 3, disclosing beads made of porous resins for immobilizing proteins or nucleic acids), (the porous resins, or alternatively, the regions containing the porous resins, are considered to be a plurality of adsorptive regions), to which ligands (i.e., the immobilized proteins in col. 37, line 6) have been bound respectively,

ii) subjecting a receptor (i.e., the particular molecule to which the immobilized proteins bind, see col. 10, lines 48-54 and 60-61 and 66-67) to specific binding with the ligands, the receptor being thereby specifically bound to the ligands [forming a ligand-receptor complex],

iii) providing a label to the ligand-receptor complex (see col. 26, line 21, disclosing an enzyme label to achieve chemiluminescence with a substrate; and see

col. 19, lines 50-55, disclosing that labels may be attached to a member of a binding complex),

iv) causing a chemical luminescence substrate (e.g., luminol substrate, col. 26, lines 20-33) to undergo a reaction with the enzyme-labeled antibody, which has been specifically bound to the labeled receptor or the labeled ligand,

wherein, a reaction liquid containing the enzyme label is forcibly caused to flow across each of the porous adsorptive regions of the biochemical analysis unit (col. 28, line 66 – col. 29, line 23, disclosing, in general, microflow through microchannels for incubation and washing steps, and a pump; and see also col. 20, col. 21, lines 23-41, disclosing pumps in microfluidic systems).

While Shipwash discloses that in general binding assays may utilize the binding between an immobilized protein to recognize an analyte to which it binds and that enzymes for chemiluminescence detection can be used, Shipwash however does not teach the particular binding assay disclosed by Applicant.

More specifically, as to claim 1, Shipwash does not disclose that the receptor is labeled, nor that the enzyme is part of an enzyme-labeled antibody wherein the enzyme-labeled antibody is subjected to specific binding with the labeled receptor. Decker et al. however teach this specific type of assay.

Decker et al. teach an improvement in an immunoassay comprising the steps of reacting an antigen bound to a solid support with a hapten/conjugated antibody to the antigen, further reacting hapten conjugated antibody bound to the solid support with labeled anti-hapten antibody and determining the labeled antibody bound to the solid

support (col. 1, lines 59-64). Decker et al. teach that the invention makes use of hapten conjugated antibodies to amplify antigenicity of the bound antibody. Each hapten conjugated antibody will have several hapten molecules bound thereto providing for multiplication of the antigenic reactivity (col. 2, lines 59-63). Moreover, Decker et al. teach that methods for directly or indirectly binding antigens or antibodies to be detected to a solid support are well known (col. 1, lines 7-11, and lines 38-40). Decker et al. also teach that the use of labeled antibodies (i.e., labeled with enzymes for example) in solid phase immunoassay is well known (col. 2, lines 43-45).

It would have been obvious to one ordinary skill in the art at the time the invention was made to perform the Decker et al. immunoassay using the Shipwash assay device because Decker et al. teach that the immunoassay as disclosed, including use of hapten/conjugated antibody, provides an improvement of the immunoassay because it amplifies the antigenic reactivity of the immunoassay. One of ordinary skill in the art would be motivated to utilize the improved immunoassay as the particular assay performed using the Shipwash assay device for its amplified detection, as would be desirable for more accurate results. Moreover, one of ordinary skill in the art would have reasonable expectation of success because Decker et al. teach that methods for directly binding antigens or antibodies to a solid support, such as the Shipwash solid support, are well known in the art. Moreover, Shipwash disclose that assays that utilize enzymes as labels may be utilized with the assay device, and thus one of ordinary skill in the art would have reasonable expectation of success in performing the assay taught by Decker et al. utilizing enzymes as labels.

Thus, in performing the Decker et al. assay method using the Shipwash assay device, the antigens bound to the solid support as disclosed by Decker et al. in column 1, lines 59-60 is considered to be the bound ligands recited by Applicant in claim 1, line 4. The hapten/conjugated antibody as disclosed by Decker in column 1, lines 60-61 is considered to be the labeled receptor recited by Applicant in claim 1, line 6. The enzyme labeled anti-hapten antibody as disclosed by Decker in column 1, line 63 is considered to be the enzyme-labeled antibody recited by Applicant in claim 1, line 13. The Office notes that Applicant has not claimed which element is an analyte intended to be detected.

As to the following claims, the limitations are disclosed by the references as follows.

As to claim 3, the steps i), ii), iii) and iv) as well as the limitations regarding the reaction liquid containing the enzyme-labeled antibody being forcibly caused to flow, as recited in claim 3, these limitations have been discussed above (see discussion of claim 1 above, including steps i) ii, iii) and iv)). The additional limitations in claim 3 regarding a reaction liquid containing the labeled receptor being forcibly caused to flow such that the reaction liquid containing the labeled receptor flows across each of the porous adsorptive regions is disclosed as follows. Shipwash discloses in general microflow through microchannels for incubation and washing steps, and a pump (see col. 28, line 66 – col. 29, line 23; and also col. 20, col. 21, lines 23-41). Moreover, Decker et al. teach an assay using a labeled receptor (i.e., hapten/conjugated antibody) as described above. Thus, in the combination of the teachings of the Decker et al. assay using the

Shipwash assay device (as discussed previously above), the step of contacting the labeled receptor with the bound ligands, as taught by Decker et al., is one of the incubation steps, that is flowed through microchannels via a pump in the Shipwash device.

3. Claims 2 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shipwash, 6,846,638, in view of Decker et al., 4,230,683, and further in view of Woias et al., 6,490,034.

Shipwash in view of Decker et al. disclose the invention substantially as claimed (see above with respect to claims 1 and 3), except for the step of ceasing fluid flow as recited in claims 2 and 4. However, Woias et al. teach the motivation to cease fluid flow.

Woias et al. teach an assay device with an inlet and an outlet and a pump that stops flow of fluid. Woias et al. teach that the device is adapted to be used in a very flexible manner, and that when an inlet and an outlet opening are provided, "stopped-flow" operation is possible. The reagent is pumped in, whereupon the pump is stopped and the reaction is allowed to take place (col. 4, lines 39-46).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to stop flow of fluid as taught by Woias et al. during performance of the Decker et al. assay utilizing the Shipwash assay device because Woias et al. teach that stopping flow of fluid allows for the reaction to take place. One of ordinary skill in

the art would recognize the benefits of stopping a pump to allow for a reaction to take place as taught by Woias et al. as it provides for more thorough completion of reaction.

Moreover, one of ordinary skill in the art would have reasonable expectation of success because Woias et al. teach that an assay device with an inlet and an outlet, and a pump, would allow for a stopped-flow operation, permitting a reaction to take place. Because the Shipwash device has a pump as well as an inlet and outlet (see for example, column 3, line 19; and see for example column 29, lines 18-19), one of ordinary skill in the art would have reasonable expectation of success in stopping the Shipwash pump to allow the reaction to take place.

More specifically, it would have been obvious to one of ordinary skill in the art at the time the invention was made to perform the Decker et al. assay using the Shipwash device such that after the reaction liquid containing the enzyme-labeled antibody has been forcibly caused to flow such that the reaction liquid flows across each of the porous adsorptive regions of the biochemical analysis unit, the forcible flowing is ceased during a period of time longer than the period of time during which the reaction liquid containing the enzyme-labeled antibody has been forcibly caused to flow, because Woias et al. teach that stopping flow allows for the reaction to take place.

Moreover, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 1-5 USPQ 233. In this case, stopping the flow of enzyme-labeled antibody for a period of time longer than the period of time during which the reaction liquid containing the enzyme-labeled antibody has been forcibly caused to

flow appears to be an optimum or workable range and thus, its discovery involves only routine skill in the art.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Liu et al., 7,005,270, disclose indirect labeling (col. 15, lines 3-15). Schoemaker et al., 4,837,167, disclose reverse sandwich assay, wherein the sample is initially incubated with labeled antibody after which the solid-phase immunoadsorbent containing immobilized antibody is added and a second incubation is carried out, thus providing the advantage of eliminating the first wash step performed in forward sandwich assays (col. 2, lies 15-35).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ann Y. Lam whose telephone number is 571-272-0822. The examiner can normally be reached on Mon.-Fri. 10-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ann Lam 5/15/06